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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/190,138
Filing Date: November 12, 1998
Appellant(s): BOSCH ET AL.

Attorney Michele M. Simkin
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 21, 2006 appealing from the Office action mailed January 14, 2004.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. The Examiner agrees with the Applicant's assertion that the appeal of 09/577,489 is unrelated to the instant application.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,985,309	Edwards	11-1999
5,202,110	Dalby	4-1993
5,145,684	Liversidge	9-1992
	Goodman & Gilman's, "The Pharmacological Basis of Therapeutics. Ninth edition," McGraw-Hill, 1996, page 666.	

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

(a) Claims 11-34, 40, 41, 44, 45, 47, 48, 51-62, 69-96, and 111-119 are rejected under 35 U.S.C. § 103(a) over Edwards et al. U.S. Patent No. 5,985,309 ("Edwards" or "'309");

'309 teaches aerosol particle compositions that are less than 100 microns in diameter and have a surface modifier adsorbed thereon. The surface modifiers can be found at column 7, lines 55-63 and in the examples and are the same as those of the instant application as stated on page 26, line 10-page 27, line 28. '309 also discloses the spray-drying and freeze-drying the compositions. Example 14 discloses that the concentration of drug is within the instant ranges (i.e. 200 μg/5mg albuterol is

equivalent to 40 mg/g). The compositions of the instant claims and those of '309 do not appear to be different. Both are aerosol compositions comprising spray- or freeze-dried drug particles less than about 100 μm, and deliver an agent to the deep lung (C 9, L 59-63). Furthermore, '309 teaches that varying the spray drying parameters, the aerodynamic properties of the inhaled particles can be effectively controlled through, for example, adjusting the inlet temperature or the feed rate and pressure of the compressed air to alter particle size (C 27, L 12-31) resulting in particle sizes that provide optimal deposition within targeted sites within the respiratory tract.

(b) Claims 11-34, 40-45, 47, 48, 51-62, 69-96, and 97-119 are rejected under 35 U.S.C. § 103(a) over Edwards et al. U.S. Patent No. 5,985,309 in view of Liversidge U.S. Patent No. 5,145,684 ("Liversidge");

where?

'309 is relied upon for all that it teaches as stated previously.

'684 teaches particle compositions that are less than 100 microns in diameter and have a surface modifier adsorbed thereon. The particles of '684 are for administration of drugs such as corticosteroids (known for treatment of asthma and allergies by administration in metered dose inhalers) and are produced by milling under non-pressurized conditions. After milling, the particles are separated from the milling dispersion. This appears to result in particles that are the same as those of the instant claims, absent a demonstration of criticality thereto.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '309 and '684 to provide aerosol corticosteroid particle formulations that meet the limitations of the instant claims based upon the motivation that corticosteroids are used in metered dose inhaler aerosol formulations for

treatment of asthma and allergies and that the rate of dissolution of a particulate drug can increase with increasing surface area, i.e., decreasing particle size, along with providing optimal deposition with targeted sites within the respiratory tract.

(c) Claims 35, 36, 49, 63, and 64 are rejected under 35 U.S.C. § 103(a) over Edwards et al. U.S. Patent No. 5,985,309 in view of Dalby et al. U.S. Patent No. 5,202,110 ("Dalby");

'309 is relied upon for all that it teaches as stated previously.

'110 is relied upon for teaching propellant metered dose inhalers where the propellant is a "non-CFC" propellant.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine '309 with '110 to provide propellant metered dose inhalers where the propellant is a "non-CFC" propellant, thereby providing "environmentally friendly" propellant compositions of the '309 compositions that provide distribution to the deep tissues of the lungs.

and (d) Claims 120 & 121 are rejected under 35 U.S.C. § 103(a) over Edwards et al. U.S. Patent No. 5,985,309 in view of Goodman & Gilman's, "The Pharmacological Basis of Therapeutics, Ninth edition, McGraw-Hill, 1996, page 666 ("Goodman").

Edwards et al (5,985,309, hereafter '309) is relied upon for all that it teaches as stated previously, including aerosol administration of steroids.

Goodman teaches that beclomethasone dipropionate is known steroid administered for asthma in aerosol formulations.

Accordingly, it would have been obvious to one skilled in the art at the time of the to administer beclomethasone dipropionate in the formulation of '309 with the motivation of providing a composition for treatment or asthma invention.

(10) Response to Argument

(a) The Applicant argues that Edwards does not teach or suggest spherical, dry powder composition of nanosized drug particles, contending that Edwards only teaches rough and amorphous non-spherical drug particles. Contrary to applicant's assertions, it is the examiner's position that the prior art as known and expressed in Edwards teaches smooth and spherical microparticle drug for inhalation (col. 9, lines 11-21). Applicant argues that the claimed dry powder aerosol comprising aggregates of spherical drug particles is a significant advance over the non-spherical single particles of drug because according to applicant, the spherical shape of particles positively influences aggregation of the drug particles and that this is crucial for the initial impact of the drug particles in the upper respiratory tract and subsequent retention in the lung. It is the examiner's position that delivery of the drug is a matter of choice and design and that whether in the form of aggregates or single particles key issue is delivering the drug in a form that can reach the alveoli of the lung. It is also noted that both the polymers comprising the micron-sized particles taught by Edwards and the therapeutic agents contained therein are obviously nanosized particles, because the size of molecules are on the nanometer length scale. Furthermore, given that the particles taught by Edwards are micron-sized, these are obviously aggregates of nanometer particles (i.e. molecules), because it is only through the association (i.e.

aggregation) of nanometer-sized molecules via intermolecular interactions that micron-sized particles could result.

Applicant asserts that the aerodynamic behavior of non-spherical drug particles would present poor airflow to upper airways of the respiratory tract. The examiner disagrees with Applicant's position, as applicant provides no evidence establishing in support of this assertion. Moreover, Edwards teaches that the nanosized drug particles in aerosol formulation can be effectively delivered to the alveoli of the lung' (abstract; col. 5, line 35 and col. 10, line 35-45). Applicant contends that the nanoparticle drug aggregates in a liquid medium must be able to redisperse in order to establish contact with and be absorbed by the nasal and pulmonary tissues arguing that there is no teaching or suggestion in Edwards that the drug particles redisperse upon contact with liquid medium. Examiner posits that applicant claims nanoparticles of drug and not a liquid dispersion medium. In this regard, it is noted that applicant indicates no specific liquid medium for dispersion of drug particles. Furthermore, examiner disagrees with applicant's position because the disclosures in Edwards teach that the drug particles may be fabricated with appropriate material, surface roughness, diameter and tap density for localized delivery to selected regions of the respiratory tract (col. 10, line 45-55) including delivery to the alveoli (col. 10, line 35 and col. 28, line 35-40). The Applicant also alleges that Edwards does not teach crystalline nanoparticulate particles. The Examiner respectfully disagrees. Edwards teaches several different therapeutic agents, including salmeterol (col. 12, line 41), which is a small molecule therapeutic, available in crystalline form. The selection of a crystalline therapeutic agent is obviously something that would have been apparent to a person of ordinary skill in the art, especially given that "recrystallization" is a commonly used purification technique of small

molecule therapeutics. It is also the Examiner's position that Edwards disclosed that nanosized drug particles in aerosol form were delivered to the alveoli of the lung (col. 3, line 330-35 and col. 5, line 30-40).

(b) Applicant argues that Liversidge does not disclose aerosol formulation of nanoparticle drugs; contending that the teaching in Edwards disclose significant difficulties respecting aerosol preparation and delivery. The Examiner disagrees with applicant's position because the disclosure in Edwards teaches:

> (1) Incorporation of surfactants into the drug particles thereby effectively reducing the tendency of the particles to agglomerate (col. 7, lines 20-45) and
>
> (2) The effective delivery of the drug particles in the lung col. 9, lines 40-60 and col. 10, lines 35-45).

While the disclosures in Liversidge hint of some level of agglutination of drug particles (col. 4, lines 60-65), it is the Examiner's position that overall, the disclosures in Liversidge are: (a) in the same field of endeavor as that in Edwards' nanosized drug particles that are surface modified in liquid dispersion (col. 3, line 45) and (b) address similar problems that were raised in Edwards concerning nanosized drug delivery formulations through the respiratory tract and therefore inhalation (col. 5, line 1 and col. 12, line 50). It is noted that both Liversidge and Edwards are indeed in the same field of endeavor, because both references teach pharmaceutical compositions, which may be administered to a subject's respiratory system (col. 8, lines 11-12 of Liversidge (i.e." oral" administration) and (e.g. Edward's abstract). Oral administration encompasses oral inhalation, and therefore administration to the respiratory system. It would

have been apparent to a skilled artisan that the two possible routes of delivery of therapeutics to the pulmonary (i.e. respiratory) system are through the nose and the mouth. Delivery through the mouth is termed "oral" and delivery via the nose is described is termed "nasal."

(c) Applicant contends that neither Edwards nor Dalby (either singly, or in combination) teach or suggest aerosol composition of nanosized drug particles. Examiner disagrees with Applicant's position in that the teaching in Edwards regarding spherical, nanosized aerosol particles of drug was discussed above (col. 4, line 40-45 and col. 9, line 65). Dalby was relied on as teaching the propellant or aerosolized formulation for delivery of nanosized beclomethasone particles, albeit no chlorofluorocarbon was used (col. 7, line 10, continuing to col. 8, line 25).

(d) In traversing the rejection of claims 120 and 121 as unpatentable over Edwards in view of the secondary reference, Goodman and Gilman ("The Pharmacological Basis of Therapeutics. Ninth edition," McGraw-Hill, 1996, page 666) Applicant argues that while Edwards does not teach or suggest the claimed aerosol composition, that Goodman also fails to address the issue regarding benefits for delivering drugs nanoparticles in aggregate formulation. The Examiner disagrees with Applicant's position in light of the discussion respecting the teachings in Edwards and further notes that Goodman teaches aerosolized formulation of glucocorticoids for delivery by inhalation (see page 666, first and second paragraphs).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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